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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/755,004 | 01/05/2001 | Anthony P. Shuber | EXT-048 | 4632 |

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|---|---|
| CHUNDURU, SURYAPRABHA | |
| ART UNIT | PAPER NUMBER |
| 1637 | 12 |

DATE MAILED: 08/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/755,004 | Applicant(s) SHUBER, ANTHONY P. | |
|---|---|---|---|
| | Examiner Suryaprabha Chunduru | Art Unit 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 17-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Applicants' response to the office action and amendment (Paper No.10) filed on May 13, 2002 has been entered. Information Disclosure Statement (Paper No. 11) has been entered.

2. Applicant's response to the office action (Paper No.10) is fully considered and deemed persuasive in part.

### New Grounds of Rejection necessitated by Amendment

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8-9, and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims 1 and 20 recite ' a reference length' and 'a reference amount' which are unclear and indefinite whether the term 'reference' refers to a control human sample nucleic acid or control patient sample nucleic acid or a control nucleic acid isolated from invitro cells. Further, Claim 18 recites 'shed cells or cellular debris' which are unclear and indefinite because it is not clear whether these terms refer to leukocytes or erythrocytes, or apoptotic cells or cellular membranes of cell organelles. Amendment of these claims to properly recite the terms would obviate this rejection.

### *Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

a. Claims 1, 6, 8, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (Digestive Diseases and Sciences, Vol. 41, No. 11, pp. 2142-2149, 1996).

With reference to the instant claim 1, Li et al. teach a method for detecting a Helicobacter pylori infection wherein the method comprises (i) detecting a helicobacter pylori nucleic acid (DNA) (417 bp in length) present in a patient stool sample by polymerase chain reaction and identifying the patient having current helicobacter pylori infection if the amount of nucleic acid exceeds (positive amplification) predetermined threshold (negative sample or no amplification) (see page 2143, column 2, paragraph 6, page 2144, column 1, paragraph 1-2, Fig 1);

With reference to the instant claims 8, 19-20, Li et al. teach (i) helicobacter pylori nucleic acid is a DNA (see page 2143, column 2, paragraph 6). Thus, the disclosure of Li et al. meets the limitations in the instant claims.

b. Claims 2-5,7, 17-18, 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Tabaqchali et al. (WO 91/09049).

Tabaqchali et al. teach a method for detecting a helicobacter pylori in a patient sample wherein,

With reference to the instant claim 2-3, and 18, Tabaqchali et al. teach that the method comprises detecting helicobacter pylori (H. pylori) nucleic acid present in a patient sample, comparing an amount of H. pylori nucleic acid present in said sample to an amount of non-helicobacter (helicobacter mustelae) nucleic acid present in said patent and identifying H. pylori

infection if relative amount of H. pylori exceeds that of non-H. pylori nucleic acid (see page 5, lines 31-37, and page 6, lines 1-3, and page 7, lines 5-16, page 20, lines 32-35). Further,

With reference to the instant claims 17, and 21, Tabaqchali et al. discloses that the method comprises amplifying a first, a second, a third H. pylori nucleic acid, detecting the amplified PCR products and identifying H. pylori infection by the presence of first, second, and third H.pylori nucleic acids in said sample (see page 10, lines 14-31, page 14, lines 1-29).

With reference to the instant claim 22-23, Tabaqchali et al. teach that the method comprises (i) exposing a patient sample to an immobilized probe that hybridizes to helicobacter pylori nucleic acids, detecting the helicobacter pylori nucleic acid which indicates the presence of helicobacter pylori infection in said patient (see page 20, lines 16-30, page 11, lines 29-34, page 5, lines 18-24); (ii) helicobacter pylori nucleic acid is 411 bp (see 14, lines 14-18).

With reference to the instant claims 5, Tabachali et al. also teaches that the patient sample could include gastric secretions and products, gastric mucosa and saliva (see page 11, lines 25-32). Thus the disclosure of Tabaqchali et al. meets the limitations in the instant claims.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over (Digestive Diseases and Sciences, Vol. 41, No. 11, pp. 2142-2149, 1996) and in view of Lapidus et al. (USPN. 6,143,529).

Li et al. teach a method for detecting a Helicobacter pylori infection wherein the method comprises (i) detecting a helicobacter pylori nucleic acid (DNA) (417 bp in length) present in a patient stool sample by polymerase chain reaction and identifying the patient having current helicobacter pylori infection if the amount of nucleic acid exceeds (positive amplification) predetermined threshold (negative sample or no amplification) (see page 2143, column 2, paragraph 6, page 2144, column 1, paragraph 1-2, Fig 1);

Li et al. teach (i) helicobacter pylori nucleic acid is a DNA (see page 2143, column 2, paragraph 6). Li et al. also teach addition of cetyltrimethylammonium bromide (CTAB) to inhibit fecal sample reactants (see page 2143, column 2, paragraph 6). However Li et al. did not teach addition of an ion chelator with concentration at least 150 mM to the stool sample.

Lapidus et al. teach a method for improving sensitivity and specificity of screening assays, wherein, Lapidus et al. teach addition of EDTA at least 150 mM, and optionally a detergent to the stool sample to improve the yield of nucleic acid from stool (see column 7, lines 28-46).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting helicobacter pylori nucleic acid in stool samples as taught by Li et al. with the method of adding EDTA as taught by Lapidus et al. because Li et al. states that 'a variety of chemicals in the fecal specimens may inhibit the PCR reaction, PCR assays of fecal samples may give false-negative results. The PCR assay of fecal specimens described here was effectively controlled to verify the inhibitory substance in the reaction mixtures. The detergent (CTAB) was added into fecal specimens to re3move PCR-inhibiting factors' (see page 2144, column 1, paragraph 3). One potential form of removal of

PCR inhibitors in stool specimens expressly motivated by Lapidus et al. is the use of EDTA, an ion chelator to enhance the yield of nucleic acid from stool samples. Further, selection of specific buffer concentration represents routine optimization with regard to reaction composition, which routine optimization parameters are explicitly recognized in Lapidus et al. As noted in *In re Aller*, 105 USPQ 233 at 235, More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the concentration of buffer selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. An ordinary practitioner would have been motivated to combine the method of Li et al. with the method of Lapidus et al. in order to achieve the expected advantage of a rapid and sensitive method for detecting Helicobacter pylori in clinical samples.

**Response to Arguments**

6. The rejection made under 35 U.S.C. 112, second paragraph in the previous office action is withdrawn herein with reference to the claims 1, 6-9 and 18 in view of the applicants' arguments and amendment (Paper No.10). The rejection is maintained for claims 2-5, since the amendment of claim 2, did not meet the requirement to over come the rejection.

7. The rejection made under 35 U.S.C. 102(b) in the previous office action, Applicant's arguments are considered but are moot in view of the new ground(s) of rejection based on the amendment.

8. With respect to the rejection made in the previous office action under 35 U.S.C. 103(a), Applicant's arguments with respect to claim 9, are considered but are moot in view of the new ground(s) of rejection based on the amendment.

No claims are allowable.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru

August 1, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER